

## **REMARKS**

### ***Status of the Claims***

Claims 1 and 4-11 are currently pending in the present application. Claim 8 has been rewritten into independent form. Claims 9-11 have been added. Support for new claims 9-11 can be found in claims 4-6. Thus, no new matter has been added. Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

### ***Provisional Request for Interview***

Further to a teleconference conducted with the Examiner on November 30, 2009, Applicants respectfully request an interview before the next Office Action is issued. As such, the Examiner is respectfully requested to contact Chad M. Rink so that an interview can be held at the Examiner's earliest convenience in order to help resolve any remaining outstanding issues.

### ***Issue under 35 U.S.C. § 103(a)***

1) Claims 1, 4, 6, and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Josephson et al. '029 (US 2003/0092029) in view of Rohr '970 (US 5,445,970) and further in view of Thompson '304 (US 2003/0190304).

2) Claims 5 and 7 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Josephson et al. '029 in view of Rohr '970 and Thompson '304 and further in view of Foster '879 (US 4,444,879).

Applicants respectfully traverse. Reconsideration and withdrawal of these rejections are respectfully requested based on the following considerations.

Legal Standard for Determining Prima Facie Obviousness

MPEP 2141 sets forth the guidelines in determining obviousness. First, the Examiner has to take into account the factual inquiries set forth in *Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), which has provided the controlling framework for an obviousness analysis. The four *Graham* factors are:

- (a) determining the scope and content of the prior art;
- (b) ascertaining the differences between the prior art and the claims in issue;
- (c) resolving the level of ordinary skill in the pertinent art; and
- (d) evaluating any evidence of secondary considerations.

*Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966).

Second, the Examiner has to provide some rationale for determining obviousness. MPEP 2143 sets forth some rationales that were established in the recent decision of *KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

As the MPEP directs, all claim limitations must be considered in view of the cited prior art in order to establish a *prima facie* case of obviousness. See MPEP 2143.03.

The Present Invention

Independent claim 1 recites:

A labeled specific binding material comprising a substance capable of specifically binding to an analyte, a spacer and magnetic beads having a diameter of 0.5 to 10  $\mu\text{m}$ , wherein the specific binding substance is coupled to the magnetic beads via the spacer and the spacer is polyalkylene glycol having 50 to 500 repeat units.

Distinctions over the Cited References

Rohr '970 recites, "The diameter of the magnetic label can preferably range from between about 0.01 microns ( $\mu\text{m}$ ) and about 1,000  $\mu\text{m}$  ... and a label can be selected based upon such factors as the analyte of interest and the desired assay protocol" (col. 12, line 61 to col. 13, line 2). This recitation indicates that the preferable value for the diameter of the magnetic particles needs to be selected from a range of about 0.01  $\mu\text{m}$  to about 1,000  $\mu\text{m}$  according to the analyte of interest and the desired assay protocol. In other words, Rohr '970 does not teach that

the diameter of the magnetic particles may be freely selected from a range of about 0.01  $\mu\text{m}$  to about 1,000  $\mu\text{m}$  regardless of the analyte of interest and the desired assay protocol or that such a diameter may be freely applied to nanoparticles disclosed in Josephson et al. '029.

Regarding the selection of the diameter of the magnetic particles, Rohr '970 recites:

Generally, small magnetic particles with a mean diameter of less than about 0.03  $\mu\text{m}$  (300 Å) can be kept in solution by thermal agitation and do not spontaneously settle.... Generally, large magnetic particles having a mean diameter greater than about 10 microns can respond to weak magnetic fields. Although large or dense labels may be used, such labels may require that the reaction mixture be stirred or agitated during the incubation steps to inhibit settling of the particles. In another embodiment, the magnetic particles can be selected to remain dispersed in the reaction mixture for a time sufficient to permit the required binding reactions without the need for a stirring or mixing means (col. 13, lines 7-25).

This recitation indicates that the small magnetic particles with a mean diameter of less than about 0.03  $\mu\text{m}$  do not require being stirred because they do not spontaneously settle. However, the large magnetic particles require being stirred in order to inhibit the settling of the particles. *The reason why the stirring for the purpose of inhibiting the settling of the particles is required is because the settling of the particles does not cause reactions.*

In such circumstances, although Rohr '970 discloses the magnetic particles with a diameter of a range of about 0.01  $\mu\text{m}$  to about 1,000  $\mu\text{m}$ , the magnetic particles which do not really require being stirred are limited to the small magnetic particles with a diameter of a range of 0.01  $\mu\text{m}$  to 0.03  $\mu\text{m}$ . In other words, if one of ordinary skill in the art uses magnetic beads having a diameter of 0.5 to 10  $\mu\text{m}$ , required in the labeled specific binding material of the present invention in view of Rohr '970, one of ordinary skill in the art would expect that they must be stirred in order to inhibit the settling thereof.

However, as disclosed in Example 2 of the present specification, 10  $\mu\text{l}$  of the magnetic bead labeled antibody solution is spotted on the surface of a polystyrene plate where the antigen is immobilized. In such circumstances, since this sample has a small amount and is not stirred, the magnetic bead is expected to settle right after the spotting. However, the high reactivity can be really provided due to PEG spacer effects.

In other words, the present invention requiring magnetic beads having the large diameter can provide high reactivity without using any stirring means. *The reason why magnetic beads having the large diameter are used in the present invention is because magnetic signals sufficient for detection are generated.*

Thus, although the present invention uses magnetic beads having the large diameter, which should settle if not stirred, the present invention can provide high reactivity without using any stirring means. As a result, the labeled specific binding material of the present invention can be also used for the detection of the samples in such a small amount that the stirring cannot be conducted, in spite of the use of magnetic beads having the large diameter.

However, Josephson et al. '029 only disclose the magnetic particles with a small diameter of less than about 1-100 nm, which do not settle without using any stirring means.

Additionally, as described above, if one of ordinary skill in the art uses magnetic beads having a large diameter of 0.5 to 10  $\mu\text{m}$ , required in the labeled specific binding material of the present invention in view of Rohr '970, one of ordinary skill in the art would expect that they must be stirred in order to inhibit the settling thereof.

Therefore, the above effects according to the present invention cannot be expected in view of Josephson et al. '029 and Rohr '970.

In such circumstances, one of ordinary skilled in the art would not arrive at the labeled specific binding material of the present invention requiring magnetic beads having a diameter of 0.5 to 10  $\mu\text{m}$  if one of ordinary skilled in the art were to combine Josephson et al. '029 and Rohr '970.

Furthermore, claim 1 recites that the labeled specific binding material contains magnetic beads having a diameter of 0.5 to 10  $\mu\text{m}$  (i.e. 500 to 10,000 nm). The Examiner admits that Josephson et al. '029 fail to disclose this element because the reference only discloses nanoparticles with an overall size of less than about 1-100 nm (paragraph [0063]). However, the Examiner relies on Rohr '970 to overcome this deficiency because Rohr '970 disclose a range of about 0.01  $\mu\text{m}$  (i.e. 10 nm) to about 1,000  $\mu\text{m}$  (i.e. 1,000,000 nm) (col. 12, lines 55-65). The Examiner then argues that one of ordinary skill in the art would combine Josephson et al. '029 and Rohr '970 based on the disclosure in column 13, lines 3-25 of Rohr '970.

However, Josephson et al. '029 explicitly disclose that the overall size of the nanoparticles is less than about 1-100 nm (paragraph [0063]). This disclosure indicates that the particles disclosed in Josephson et al. '029 must be nanoparticles with a diameter of less than about 1-100 nm.

In such circumstances, if one of ordinary skill in the art were to combine Josephson et al. '029 and Rohr '970, one of ordinary skill in the art would expect nanoparticles with the diameter of 10-100 nm which is included in both Josephson et al. '029 and Rohr '970. In other words, one of ordinary skill in the art would not expect magnetic beads having a diameter of more than 100 nm, i.e. 0.5 to 10  $\mu$ m, as recited in claim 1.

As discussed above, Josephson et al. '029 in view of Rohr '970 do not disclose each and every aspect of claim 1, from which all other claims ultimately depend. Applicants respectfully submit that Thompson '304 and Foster '879 do not overcome the deficiencies of these references.

To establish a *prima facie* case of obviousness of a claimed invention, all of the claim limitations must be disclosed by the cited references. As discussed above, the cited references fail to disclose all of the claim limitations of independent claim 1, and those claims dependent thereon. Accordingly, the combination of references does not render the present invention obvious.

Furthermore, the cited references or the knowledge in the art provide no reason or rationale that would allow one of ordinary skill in the art to arrive at the present invention as claimed. Therefore, a *prima facie* case of obviousness has not been established, and withdrawal of the outstanding rejections is respectfully requested. Any contentions of the USPTO to the contrary must be reconsidered at present.

### **New Claims 9-11**

Applicants have newly added claims 9-11 in an effort to further define the scope of protection owed to Applicants. Applicants respectfully submit that claims 9-11 are allowable for the reasons given above. As such, Applicants respectfully assert that claims 9-11 clearly define over the cited references, and an early action to this effect is earnestly solicited.

### CONCLUSION

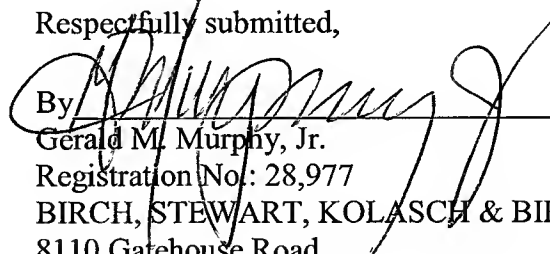
A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case clearly indicating that each of claims 1 and 4-11 are allowed and patentable under the provisions of title 35 of the United States Code.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Chad M. Rink, Reg. No. 58,258 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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